**Title**: [title]

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1 Afiliación, lugar.

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## Abstract

**Objective**: […]. **Material and methods**: […]. **Results**: […]. **Conclusion**: […].

**Keywords**: […].

# Introduction

[…].

[…].

[…].

# Material y methods

## Participants

[…].

## Instruments

### Instrument 1

[…].

### Instrument 2

[…].

## Procedures

[…].

[…].

## Statistical analysis

Data is presented as median (*Mdn*) and interquartile range (*IQR*) for continuous variables; for categorical/discrete variables, the absolute and relative sample size was reported.

A non-parametric approach was used since the underlying distribution of continuous measured outcomes, assessed through analytical and graphical methods, did not follow a Gaussian distribution.

In order assess the differences in developmental scores between males and females, the *Wilcoxon* rank-sum test was used, meanwhile the chi-square test () was used to evaluate the goodness-of-fit () and the independence of factors ().

Generalized additive models (GAM) were used to describe linear and non-linear relationships in the form of smooth terms between developmental characteristics, represented through penalized regression splines ([1](#ref-wood2011fast)). Restricted maximum likelihood (i.e., REML) method was used for the estimation of the smoothing parameters, and thin-plate regression splines for smoothing basis, as they are the optimal smoother of any given basis dimension/rank ([2](#ref-wood2003thin)). To describe the smooth terms by means of quasi-linear segments, we used approximative effect derivatives to summarise the trend with 95% confidence intervals.

To account for any source of variability coming from subject’s sex, evaluators and the type of relationship between the infants with the respondents, we incorporate them as random effects in the fitted models in the form of penalized parametric terms ([3](#ref-wood2016smoothing)).

A probability of committing a type I () error of less than 5% (*p* < 0.05), was considered sufficient evidence for statistical significance in hypothesis testing. All the statistical analyses were computed and implemented in the R programming language ([4](#ref-rlanguage)). GAMs and the corresponding model estimates were computed using the *mgcv* and *modelbased* packages with their corresponding documentation ([5](#ref-wood2017generalized),[6](#ref-dominique2020estimation)). Complementary R packages were used for visualization purposes ([7](#ref-hadley2016ggplot2),[8](#ref-daniel2021see)).

# Results

From a total of 234 subjects with congenital hypotonia, 94 (40.2%) were females and 140 (59.8%) males ( (1) = 9.04, *p* = 0.003, = 0.19, CI0.95%[0.09, 1]). The developmental characteristics of the sample can be seen in [Table 1](#tab1).

When modelling the effect of chronological age corrected for prematurity on developmental domains, we observed a significant non-linear relationship on communication scores ( (5.2, 224.04) = 13.43, *p* < 0.001), that reflect an overall negative marginal effect ( = -2.36, CI95%[-3.47, -1.25], (224.04) = -4.2, *p* < 0.001), however, this was not true when assessing the direction of the effect in the age range between 1 to 7 ( = 0.49, CI95%[-0.89, 1.86], (224.04) = 0.45, *p* = 0.319), and neither in the 18 to 48 months old group ( = 0.45, CI95%[-1.32, 2.23], (224.04) = 0.42, *p* = 0.593), whereas the effect tend to be positive but non-significant.

When analyzing the motor skills domain we found a significant non-linear effect of corrected age on gross motor scores ( (5.24, 226.75) = 6.19, *p* < 0.001), which had an overall positive effect ( = 1.95, CI95%[0.66, 3.25], (226.75) = 2.97, *p* = 0.003), nevertheless, the slope varied across age, whereas between the 0 to 7 age range this has a negative effect on gross motor score = -2.94, CI95%[-4.55, -1.34], (226.75) = -3.7, *p* = 0.004, but in the 9.7 to 15.5 a positive effect was observed ( = 1.86, CI95%[0.61, 3.11], (226.75) = 2.93, *p* = 0.009), meanwhile in the 7.3 to 9.2 ( = 0.02, CI95%[-1.12, 1.17]) and 16 to 48 months old ( = -0.02, CI95%[-2.05, 2.01]) the slope was non significant and practically cero ( (226.75) = 0.06, *p* = 0.45, and (226.75) = 0.07, *p* = 0.646 respectively).

The relationship between developmental domains and corrected age can be seen in [Figure 1](#fig1).

# Discussion

[…].

[…].

[…].

# Conclusion

[…].

# Acknowledgment

[…].

# Conflicts of interest

[…].

# References

1. Wood SN. Fast stable restricted maximum likelihood and marginal likelihood estimation of semiparametric generalized linear models. Journal of the Royal Statistical Society (B). 2011;73(1):3–6.

2. Wood SN. Thin-plate regression splines. Journal of the Royal Statistical Society (B). 2003;65(1):95–114.

3. Wood SN, N., Pya, S"afken B. Smoothing parameter and model selection for general smooth models (with discussion). Journal of the American Statistical Association. 2016;111:1548–75.

4. R Core Team. R: A language and environment for statistical computing [Internet]. Vienna, Austria: R Foundation for Statistical Computing; 2021. Available from: <https://www.R-project.org/>

5. Wood SN. Generalized additive models: An introduction with r. 2nd ed. Chapman; Hall/CRC; 2017.

6. Makowski D, Ben-Shachar MS, Patil I, Lüdecke D. Estimation of model-based predictions, contrasts and means. CRAN [Internet]. 2020; Available from: <https://github.com/easystats/modelbased>

7. Wickham H. ggplot2: Elegant graphics for data analysis [Internet]. Springer-Verlag New York; 2016. Available from: <https://ggplot2.tidyverse.org>

8. Lüdecke D, Patil I, Ben-Shachar MS, Wiernik BM, Waggoner P, Makowski D. [see: An R package for visualizing statistical models](https://doi.org/10.21105/joss.03393). Journal of Open Source Software. 2021;6(64):3393.

**Table 1**. Overall baseline and developmental characteristics of the sample and grouped by sex. 1 Data is presented as sample size, and *Mdn* (*IQR*); 2 P-values derived from the *Wilcoxon* rank-sum test.

**Figure 1**. Relationship between corrected age (in months) and developmental domains. Regression lines and shaded area represent predicted values estimated from GAM models and their 95% confidence interval. Points and error bars represent the mean and standard error at 5-month age intervals.